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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,777	07/13/2001	James Chen	25886-0057	5768

20985 7590 05/22/2006

FISH & RICHARDSON, PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,777	CHEN, JAMES	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-21 and 25-28* is/are pending in the application.

4a) Of the above claim(s) *13,14 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-12,15-21,25,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/3/01 7/20/04 9/21/04 4/4/02 10/6/03 7/25/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicant election with traverse of the species of chlorin. After review and reconsideration of the claims in light of the prior art, the election of species Requirement, mailed Nov 18, 2005, is withdrawn. Re-acknowledgment is made of applicant election without traverse of the species of antibody which binds to tumor surface antigen in the reply filed Aug 19, 2005. It is noted that in said reply applicant indicates that claims 1-12, 14-21, 25, 27 and 28 read on the elected species, however, claim 14 is dependent on claim 13 which is a non-elected claim. In order to advance prosecution, it is assumed that the inclusion of claim 14 was a typographical error.

Claims 1-21 and 25-28 are pending. Claims 13, 14 and 26, drawn to non-elected species, are withdrawn from consideration. Claims 1-12, 15-21, 25, 27 and 28 and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 and 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) The term "low fluence rate" in claims 1 and 2 is a relative term which renders the claim indefinite. The term "low fluence rate" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification states

What is meant by "relatively low fluence rate" is a fluence rate that is lower than that typically used and one that generally does not result in significant damage to collateral or non-target tissues. Specifically, the intensity of radiation used to treat the target cell or target tissue is

preferably between about 5 and 100 mW/cm..sup.2. More preferably, the intensity of radiation is between about 10 and 75 mW/cm..sup.2. Most preferably, the intensity of radiation is between about 1 and 50 mW/cm..sup.2.

Relying on that which is "typically used" and "that which generally does not" fails to set the metes and bounds of the claim because this requires a subjective judgment on the part of a routineer to determine what is typical versus that which deviates from the typical, and what is general versus that which deviates from the general. Further, the recitation of the preferable conditions of between 5 and 100mW/cm2, 10-75mW/cm2 and 1-50mW/cm2 constitutes preferred embodiments and does not suffice as a limiting definition for the claims.

(B) Claim 3 recites "other types of fluorescent lights" and "other electroluminescent devices". It is unclear what the term "other" is an alternative to. for purpose of examination claim 3 will be read as including all fluorescent and electroluminescent light sources.

(C) Claim 2 recites "a second member of the ligand-receptor binding pair conjugated to a photosensitizing agent or a photosensitizing agent delivery system or prodrug". It is noted that photosensitizing agent or a photosensitizing agent delivery system or prodrug are all referred to in the alternative. Thus, this second conjugate does not require a photosensitizing agent because the third alternative is simply a "prodrug". It is therefore unclear how the subsequence method step of "irradiating at least a portion of the subject with light at a wavelength absorbed by the photosensitizing agent" is acted upon in the case where the second conjugate comprises a prodrug which is not a photosensitizing agent. For purpose of examination, claim 2 will be read in light of a prodrug which is a photosensitizing agent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-12, 15-21, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method comprising a pretargeting system for the delivery of photosensitizing agents to tumor cells in the vascular system, does not reasonably provide enablement for a method comprising the delivery of photosensitizing agents which are prodrugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claim 2 is drawn in part to a method which requires the administration of a ligand-receptor binding pair conjugated to a photosensitizing prodrug. Claims 2-12, 15-21, 27 are broadly drawn to encompass a prodrug form of any photosensitizing agent which could be used within the claimed methods. Claim 28 encompasses specific classes of photosensitizers, such as chlorins, bacteriochlorins phthalocyanines, porphyrins, purpurins, merocyanines, psoralens benzoporphyrin derivatives, each of which encompass a genus of photosensitizing compounds.

The specification does not provide a synthetic methodology for the construction of a prodrug derivative for any photosensitizing agent encompassed by the claims. the specification fails to provide teachings regarding the appropriate protecting groups, nor does the specification teach the linking strategy of the protected photosensitizing group with the ligand-receptor binding pair, nor the appropriate conditions for removal of the protecting groups. Further, it is noted that although one of skill in the art could design synthetic strategies o produce the required compounds, it is necessary to empirically test the strategy in order to assure that the material can be made in a manner to produce the actual compound (Warren, Organic Synthesis: The Disconnection Approach, 1982, page xi, lines 9-14 under the heading of "Introduction") and an amount of the actual compound which could be used in a treatment of mammalian patients commensurate with the scope of the claims, results from the synthesis. It is noted that Warren teaches that the art is unreliable, specifically pointing out that results different from those which are expected are not unusual. Thus, one of skill in the art would .be subject to undue experimentation in order to designing synthetic strategies and produces the claimed compounds in yields that would be adequate to use in a prodrug strategy for treating mammalian patents as required by the instant methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 9-12, 19-21, 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richter et al (U.S. 5,484,803) in view of Schultes et al (SPIE, 1994, Vol. 148, pp. 148-157), Kubler et al (U.S. 5,529,903) and Racila et al (PNAS, April 1998, vol. 95, pp. 4589-4594).

Claim 1 is drawn to a method of destroying or impairing target cells that comprise a lesion in the vascular system of a mammalian subject n comprising administering to a subject a therapeutically effective amount of a photosensitizing agent , wherein the photosensitizing agent is conjugated to a ligand that selectively binds to a receptor on target cells of the lesion and irradiating at least a portion of the subject with light at a wavelength absorbed by the photosensitizing agent wherein the light source is provided by a light source that is external to the intact body of the subject , the irradiation is at a relatively low fluence rate that results in the activation of the photosensitizing agent and the photosensitizing agent is cleared from the skin and subcutaneous tissues of the subject prior to the irradiation. Claim 3 embodies the method of claim 1 wherein said light source is selected from a group consisting of one or a plurality of laser diodes, fiber lasers, LEDs, non-laser light, cold cathode fluorescent tube, incandescent lights, halogen lights, polymeric luminescent devices, other types of fluorescent lights, discharge lamps and other electroluminescent devices. Claim 4 embodies the method of claim 1 wherein said light is directed through the skin and parallel to the wall of a vascular vessel having the lesion. Claim 9 embodies the method of claim 1 wherein the photosensitizing agent absorbs light in the range of 600nm to 1100 nm. It is noted that the "delivery system" or "prodrug" requirement of claim 9 is optional. Claim 28 embodies the method of claim 9 wherein the photosensitizing agent is selected from the groups consisting of chlorin, bacteriochlorins, , phthalocyanines, ,

porphyrins, purpurins, merocyanines, psoralens, BPD, sodium porfimer, amino levulinic acid, indocyanine green, methylene blue, toluidine blue and texaphyrins. Claim 10 embodies the method of claim 1 wherein said wavelength is from about 600nm to about 1100nm. Claim 11 embodies the method of claim 10 wherein said wavelength is greater than about 700nm. Claim 12 embodies the method of claim 11 wherein said light results in a single photon absorption mode by the photosensitizing agent. Claim 19 embodies the method of claim 1 wherein said subject is irradiated with a total fluence of about 30 joules to about 25, 000 joules. Claim 20 embodies the method of claim 1 wherein said subject is irradiated with a total fluence of about 100 joules to about 20, 000 joules. Claim 21 embodies the method of claim 1, wherein said subject is irradiated with a total fluence of about 500 joules to about 10, 000 joules. Claim 25 embodies the method of claim 1 wherein the ligand is an antibody or an antibody fragment specific to a tumor surface antigen.

Richter et al teach a method for a method of destroying or impairing blood-borne target cells that have selectively accumulated a photosensitizing agent while leaving non-target cells relatively unimpaired comprising applying radiation transcutaneously to at least a portion of an intact animal at an intensity to selectively impair or destroy target cells (column 2, line 62 to column 3, line 1), wherein target cells include cells undergoing rapid division as compared to non-target cells. Richter et al teach the transcutaneous administration of radiation to at least a portion of a subject at an intensity effective to impair or destroy target cells which have accumulated a photosensitizing agent relative to non-target cells (column 4, lines 14-21). Richter et al teach the use of preferred photosensitizing agents which are the photosensitizing agents recited in the instant claim 28 (column 4, lines 24-30), Richter et al teach that the preferred wavelength for exciting the photo-conjugate is in the range of 600-900-nm (column 3, lines 57-59) which fulfills the limitations of claims 9-11. Richter et al teach that the preferred wavelength matches the excitation wavelength of the photosensitizer agent (column 3, lines 55-56) which fulfills the limitation of claim 12 because the absorption of a single photon of light at the exact excitation wavelength by one molecule comprising photosensitizer will be a single photon absorption excitation of said photosensitizer. Richter et al teach that the intensity of radiation to the bloodstream is preferably between about 2 and 150 mW/cm2, 10 to 100mW/cm2 and 15-70mW/cm2, which satisfied the specific limitation of claim 1 with regard to "relatively

low fluence". Richter et al teach that the duration of the radiation exposure is between 0.25 minute and 24 hours which fulfills the specific limitations with regard to total fluence in claims 19-21. Richter et al teach that the photosensitizer may be conjugate with an immunoglobulin or immunospecific fragments of immunoglobulins to permit more concentration of the photosensitizing agent at the target cells (column 4, lines 39-47), although Richter et al teach that BPD has a higher affinity for tumor tissue including leukemic cells than non-tumor tissue. Richter et al teach the use of red light for the activation of BPD in the blood thus fulfilling the specific limitation of claim 3, requiring other electroluminescent devices. Richter et al teach that a preferred embodiment is the irradiation of areas with blood vessels close to the surface (column 4, lines 16-18). Richter et al do not specifically teach the combination of an antibody conjugated photosensitizing agent and the targeting of lesions in the vascular system by said antibody-photosensitizer conjugate, or the physical direction of the light parallel to a blood vessel containing the target cells.

Schultes et al teach a photodynamic laser therapy in patients having extended chest wall metastases of primary breast carcinoma comprising the administration of antibody-coupled phthalocyanines including anti-MCA or anti-TAG 72 antibodies , followed by irradiation at 675 nm, 50J/cm2 light 72-90 hours after intravenous injection (page 150, section 2.6) which meets the specific limitation of claim 1 requiring that the photodynamic agent is cleared from the skin and subcutaneous tissues prior to the irradiation. Schultes et al teach that the therapy was useful as a palliative treatment because of the reduction in metastasis and pain (page 155, section 3.7). Schultes et al teach that administration of the antibody conjugated photosensitizer versus the photosensitizer alone, allows for a reduction in the dose of photosensitizer used and the more selective binding to target cells allows for reduced cutaneous photo toxicity (page 156, lines 24-31).

Kubler et al (U.S. 5,529,903) teach the necessity of destroying circulating cancer cells in the blood stream (column 1, lines 24-27 and lines 31-35).

Racila et al (PNAS, April 1998, vol. 95, pp. 4589-4594) teach a method of detecting circulating breast cancer cells in the blood of cancer patients comprising labeling with antibodies which specifically bind to epithelial cells, such as anti-mucin-1 and anti-cytokeratin (page 4591, column 1, lines 1-6 and under the heading of "figure 3").

It would have been prima facie obvious at the time the claimed invention was made to make a antibody-photosensitizing agent conjugate comprising the photosensitizing agents taught in the method of Richter et al and the antibodies taught by Racila et al and use said conjugates in a method of photodynamic therapy to kill circulating breast cancer cells in breast cancer patients as suggested by Schultes et al. One of skill in the art would have been motivated to do so by the teaching of Schultes et al suggesting that photodynamic therapy can aid patients by reducing metastatic load and thereby reducing pain, and the teaching of Kubler et al which reflect the consensus in the art that destruction of circulating tumor cells in the blood stream would impede the metastatic spread of a tumor. Further, it would have been obvious to direct the excitation wavelength of light parallel to the wall of a blood vessel harboring a breast tumor or micro foci in order to activate the photosensitizing agent attached to the tumor cells by means of the antibody and avoid damage to normal cells of the blood vessel because Richter et al teaches the irradiation of a blood vessel close to the surface and the necessity of avoiding damage to the normal portion of the blood vessel.

Claims 1-4, 9-12, 15-17, 19-21, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richter et al, Schultes et al, Kubler et al (U.S. 5,529,903) and Racila et al as applied to claims 1, 3, 4, 9-12, 19-21, 25 and 28 above, and further in view of Theodore et al (WO 95/15979).

The specific embodiments of claims 1, 3-12, 19-21, 25 and 28 are recited above.

Claim 2 is drawn to A method for destroying or impairing target cells that comprise a lesion in the arterial vascular system in a mammalian subject comprising: administering to the subject a therapeutically effective amount of a first conjugate comprising a first member of a ligand-receptor binding pair conjugated to an antibody or antibody fragment, wherein said antibody or antibody fragment selectively binds to a target cell or target tissue antigen; administering to the subject a therapeutically effective amount of a second conjugate comprising a second member of the ligand-receptor binding pair conjugated to a photosensitizing agent or photosensitizing agent delivery system or prodrug, wherein the first member binds to the second member of the ligand-receptor binding pair; irradiating at least a portion of the subject with light at a wavelength absorbed by said photosensitizing agent, wherein said light is provided by a light

source that is external to the subject; and wherein said irradiation is at a relatively low fluence rate that results in the activation of said photosensitizing agent or prodrug product. Claim 15 embodies the method of claim 2, wherein said target tissue antigen is selected from the group comprising a tumor surface antigen. Claim 16 embodies the method of claim 2, wherein said ligand-receptor binding pair is selected from the group consisting of: biotin-streptavidin; chemokine-chemokine receptor; growth factor-growth factor receptor; and antigen-antibody. Claim 17 embodies the method of claim 9 wherein said photosensitizing agent delivery system comprises a liposome delivery system. Claim 27 embodies the method of claim 2 further comprising administering to said subject a liposomal delivery system separately conjugated to the second member of the ligand-receptor pair

Theodore et al teach a method of increasing photosensitizing active agent localization at a target cell site within a mammalian recipient, which method comprises: administering to the recipient a first conjugate comprising a targeting moiety and a member of a ligand-antiligand binding pair, wherein the first conjugate localizes at a target site; and administering to the recipient a second conjugate comprising a photosensitizing agent and a ligand/antiligand binding pair member, wherein the second conjugate binding pair member is complementary to that of the first conjugate, and wherein the photosensitizing agent or the second conjugate is chemically modified to induce rapid renal clearance thereof from the recipient. Theodore et al teach that the photosensitizing agent absorbs light at wavelengths ranging from about 600 to about 800 nm, and the photosensitizing agent is selected from the group consisting of porphyrin derivatives with a strong absorption band between 600 and 700 nm; phthalocyanines chelated with aluminum or zinc; an ether/ester derivative of porphyrin; chlorins; purpurins; and benzoporphyrin derivatives (claims 17-20). Theodore et al teach the delivery of photosensitizing agent to target cells through the pretargeting approach using ligand or antigen derivatized liposomes (page 102, lines 24-30 and page 113, line 29 to page 114, line 11).

It would have been prima facie obvious at the time the claimed invention was made to use a pretargeting system for the administration of the photosensitizer in a method to kill tumor cells in the vascular system of a mammalian subject, and to use liposomes loaded with said photosensitizer wherein said liposomes are attached to a ligand of the pretargeting system. One

of skill in the art would have been motivated to do so by the teachings of Theodore et al on the improvements in targeting tumor cells by using pretargeting system rather than direct targeting.

Claims 1, 3, 9-12, 18-21, 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abels et al (WO 97/31582) in view of the abstract of Goetz et al (WO 97/33620) and Schultes et al (SPIE, 1994, Vol. 148, pp. 148-157).

Claim 18 embodies the method of claim 1 wherein said light source is pulsed modulated to maximize the depth of tissue penetration and minimize heat generation and power consumption.

Abels et al teach a photodynamic method for treating highly vascularized tumors and their metastases, such as Kaposi's sarcoma; adenocarcinoma of the colon, esophagus, breast; neurofibroma and malignant melanoma (page 8, line 22 to page 9, line 11) comprising administering indocyanine green (ICG), followed by irradiation with light, either continuous or pulsed, at a substantially lower intensity than used with photothermal therapy (page 10, lines 11-14 and lines 18-20) which fulfills the specific limitation of claim 18. Abels et al teach a light source which is a laser diode (page 15, lines 1-3) which fulfills the specific limitation of claim 3. Abels et al teach fluence rates of less than 10W/cm2, including 5mW/cm2 to 5W/cm2, 10mW/cm2 to 3W/cm2, 25mW/cm2 to 2W/cm2 and 40mW/cm2 to 500mW/cm2, and for deeper tumors, 2W/cm2 to 5W/cm2 (page 8, lines 14-21). Abels et al teach that a typical total light dose is 100j/cm2 but that the dose can vary from 10J/cm2 to 200J/cm2 (page 14, lines 18-20) and that a diode laser can be used anywhere in the range of 770-840nm, but preferably at 805nm or 800nm because 800nm is the wavelength at which absorption of light by body pigments and blood is negligible allowing light penetration to greater depths (page 15, lines 1-10). It is noted that 805nm is the absorption maximum of ICG (page 3, lines 4-6) and thus irradiation at 805nm fulfills the limitation of claim 12, requiring a single photon absorption mode. Abel et al rely on the natural accumulation of ICG within the microcirculation of oncological lesions (page 3, lines 11-22). Abel et al do not teach the conjugation of ICG with a tumor targeting antibody.

Schultes et al teach that administration of the antibody conjugated photosensitizer versus the photosensitizer alone, allows for a reduction in the dose of photosensitizer used and the more

selective binding to target cells allows for reduced cutaneous photo toxicity (page 156, lines 24-31).

The abstract of Goetz et al teaches an IGC antibody conjugate for the treatment of tumors.

It would have been prima facie obvious at the time the invention was made to administer ICG conjugated to an antibody which binds to a tumor surface antigen for localization of ICG at the tumor site. One of skill in the art would have been motivated to do so by the teachings of Schultes et al on the reduction of cutaneous toxicity associated with antibody conjugated photosensitizer versus photosensitizer as a single agent and the teachings of the abstract of Goetz et al on the ICG-antibody conjugate for the treatment of tumors.

Claims 1-3, 9-12, 15-21, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abels et al (WO 97/31582) and the abstract of Goetz et al (WO 97/33620) and Schultes et al (SPIE, 1994, Vol. 148, pp. 148-157) as applied to claims 1, 3, 9-12, 18-21, 25 and 28 above, and further in view of Theodore et al (WO 95/15979).

Abels et al teach the administration of ICG in a liposomal preparation (page 9, line 17 to page 9, line 2). However the combination of Abels et, Schultes et al and Goetz et al does not render obvious the administration of a photosensitizing agent delivery system comprising a first and second antibody conjugate pair.

Theodore et al teach a method of increasing photosensitizing active agent localization at a target cell site within a mammalian recipient, which method comprises: administering to the recipient a first conjugate comprising a targeting moiety and a member of a ligand-antiligand binding pair, wherein the first conjugate localizes at a target site; and administering to the recipient a second conjugate comprising a photosensitizing agent and a ligand/antiligand binding pair member, wherein the second conjugate binding pair member is complementary to that of the first conjugate, and wherein the photosensitizing agent or the second conjugate is chemically modified to induce rapid renal clearance thereof from the recipient. Theodore et al teach that the photosensitizing agent absorbs light at wavelengths ranging from about 600 to about 800 nm, and the photosensitizing agent is selected from the group consisting of porphyrin derivatives with a strong absorption band between 600 and 700 nm; phthalocyanines chelated with

aluminum or zinc; an ether/ester derivative of porphyrin; chlorins; purpurins; and benzoporphyrin derivatives (claims 17-20). Theodore et al teach the delivery of photosensitizing agent to target cells through the pretargeting approach using ligand or antigen derivatized liposomes (page 102, lines 24-30 and page 113, line 29 to page 114, line 11).

It would have been prima facie obvious at the time the claimed invention was made to use a pretargeting system for the administration of ICG in a method to kill the highly vascularized tumor cells as taught by Abels et al, and to use liposomes loaded with said photosensitizer wherein said liposomes are attached to a ligand of the pretargeting system. One of skill in the art would have been motivated to do so by the teachings of Theodore et al on the improvements in targeting tumor cells by using pretargeting system rather than direct targeting, the further specific teaching of Theodore et al on the targeting of antigen-derivatized liposomes which could be used in the pretargeting system and the suggestion by Abels et al that ICG be administered in a liposomal preparation.

Claims 5-8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

5/13/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER